REMARKS

Claim Rejections – 35 U.S.C. §102

Claim 21 was rejected under 35 U.S.C. §102(b) as being anticipated by Rothberg et al. (U.S. Patent No. 5,972,693).

The Examiner states Rothberg et al. teaches a kit for amplifying cDNA comprising DNA ligase, a DNA polymerase, a reverse transcriptase without RNase H activity, an enzyme for degrading mRNA from CDNA-mRNA hybrid, and four deoxynucleoside triphosphates and sequence specific primers (see column 26, lines 56-67, column 27, lines 100, lines 17-37). Thus, the Examiner states the disclosure of Rothberg et al. meets the limitations in the instant claim.

Applicants have cancelled claim 21, thus alleviating this rejection.

Claim Rejections – 35 U.S.C. §103

The Examiner states this application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. §103(a), the Examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the Examiner to consider the applicability of 35 U.S.C. §103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C 103(a).

Applicants acknowledge their obligation under 35 CFR 1.56 to point out the inventor and the invention dates of each claim that was not commonly owned at the time a later invention was made.

Claims 1, 3-17, 26-27 were rejected under 35 U.S.C. 103(a) as being unpatentable under Hu et al. (U.S. Patent No. 6,203,984) in view of Li et al. (U.S. Patent No. 6,399,334).

The Examiner states it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made, to combine the method of amplifying cDNA as taught by Hu et al. with the reverse transcriptase RNase H⁻ as taught by Li et al. to achieve expected advantage of developing an efficient amplification method because Li et al. suggests that "the invention provides removal of contaminating or background nucleic acid molecules from the normalized library, and such removal or elimination of contaminating nucleic acids might be performed prior to or after normalization" (see column 15, lines 9-26). The Examiner asserts an ordinary practitioner would have been motivated to combine the teachings of Hu et al. with the method of Li et al. to achieve a sensitive method of the amplifying cDNA by incorporating the reverse transcriptase RNase H⁻ because this limitation would improve the elimination or reduce background contamination.

Applicants traverse this rejection. There is no suggestion in the prior art represented by the references that they be combined in the manner proposed by the Examiner. Absent such a suggestion, there would be no reason why one skilled in the art and who had no prior knowledge of Applicants' claimed method, would consult this particular combination of references suggested by the Examiner. As stated by the Examiner, Hu et al. did not specifically teach a reverse transcriptase without RNase H⁻ activity, because Hu shows no recognition to the problem of circumventing the requirements to synthesize double stranded cDNA following reverse transcription of mRNA to first strand cDNA. Applicants teach it is more difficult to obtain full-length double stranded cDNA than to obtain full length first, single strand cDNA. Applicants' novel method is directed at amplification of a polynucleotide which includes amplification of the

3′ and 5′ ends of the molecule. Applicants use only first strand cDNA as the PCR template, so that the longest first strand cDNA can be synthesized by using reverse transcriptase without RNase H activity, therefore one skilled in the art would not be likely to use Hu alone or in combination with Li in an attempt to solve such a problem. In any event, the method that results from the Examiners proposed combination of references would not meet Applicants claimed method.

The Examiner has failed to make a prima facie showing of obviousness because the references fail to teach all of the claim limitations. Applicants respectfully submit that Hu et al. does not teach step (v) as proposed by the Examiner. That Examiner asserts that Hu teaches in step (v), introducing first and second specific primers to set circular cDNA and amplifying the cDNA used in primer extension amplification (see column 2, lines 4-26, column 11, lines 1-28). Hu fails to teach the limitation of amplifying a first strand cDNA using two specific PCR primers wherein the primers are designed such that each primer has a 3′ end toward either the 5′ end or the 3′ end of the circular cDNA (see spec. page 10, lines 14-17). (See Fig. 1 and claims 10 and 11).

Instead Hu et al. teaches a method of making cDNA that comprises incubating mRNA with reverse transcriptase enzyme and a primer in a 5′ to 3′ orientation. The second primer is not added until after ligation (see e.g., column 9, lines 10-14.) Moreover, Hu's method is directed at making a cDNA not amplification of the cDNA to obtain full-length strands.

Conversely, Applicants' method comprises obtaining mRNA; reverse transcribing mRNA; degrading mRNA complex; ligating the cDNA ends; then introducing first and second sequence specific primers to the circular cDNA. This would not be obvious to one of ordinary skill in the art as the primers are designed so that each one has a 3′ end toward either the 5′ end or

the 3′ end of the circular cDNA (see spec. page 10, lines 14-17). (See claims 10 and 11). This means that the forward primer will typically be towards the 3′ end of the molecule and the reverse primer would be towards the 5′ end of the molecule (see spec. page 10, lines 17-19). See Figure 1. PCR or another primer extension procedure is used to re-amplify the resulting specific nucleotide sequence the resulting amplified product will thus include the desired 3′ and 5′ ends of the cDNA outside of the two primers. In other words, amplification is performed by using TWO specific PCR primers. Since Hu fails to teach this limitation the Examiner has failed to make a *prima facie* showing of obviousness.

Applicants have amended claims 26 and 27 by adding dependent claims which include the limitations of having primers designed so that each one has a 3′ end toward either the 5′ end or the 3′ end of the circular cDNA. Again, Hu et al. fails to teach this limitation. Applicants respectfully request the Examiner to withdraw the rejections to claims 26 and 27.

No fees or extensions of time are believed to be due in connection with this amendment; however, consider this a request for any extension inadvertently omitted, and charge any additional fees to Deposit Account No. 26-0084.

Reconsideration and allowance is respectfully requested.

Respectfully submitted,

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